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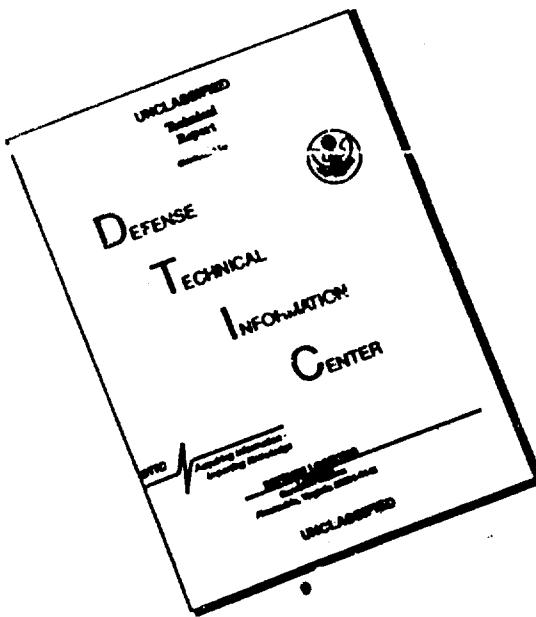
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# ON THE MECHANISM GOVERNING THE REACTION OF QUINONES
WITH HYDROXYL IONS

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The mechanism governing the reaction of quinones with a hydroxyl ion has been extensively discussed in the literature in relation to a recently presented hypothesis (1) on the participation of this reaction as a link in enzyme processes that are involved in the storage and transfer of energy in biological systems. The authors of this hypothesis (1) have postulated the following mechanism for the reaction of quinones with the hydroxyl ion[1]

$$2OH \longrightarrow H_2O_2 \qquad\qquad 1,6$$
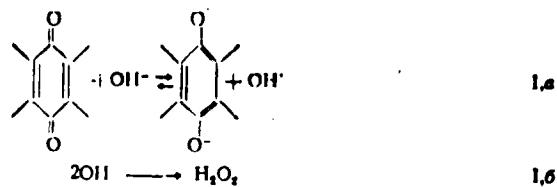
In this paper we discuss another mechanism for this reaction, which we consider as more probable (2):

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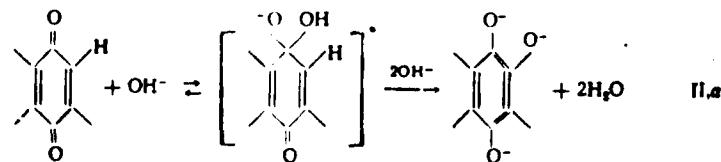
[1]Somewhat earlier, a similar mechanism was proposed without any substantiation also in the work (3).

$$2 \overset{\text{O}}{\underset{\text{O}}{\bigcirc}}{}^{H} + \underset{\text{O}}{\overset{\text{O}^-}{\bigcirc}}{}^{\text{O}^-} \longrightarrow 2 \underset{\text{O}^-}{\overset{\text{O}^-}{\bigcirc}}{}^{H} + \underset{\text{O}}{\overset{\text{O}}{\bigcirc}}{}^{\text{O}^-} \quad \text{II}$$
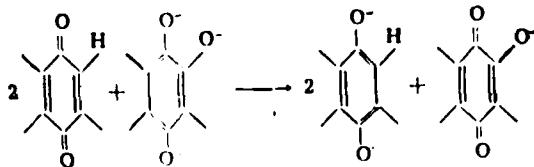
Occurrence of the reaction under scheme I in accordance with the above-stated hypothesis assumes the existence in organisms of such redox processes in which water, and not ordinary biological biological substrates, acts as the reducing agent. We can see that mechanism II excludes the possibility of the participation of the reaction under study in enzymatic processes, since it presumes an irreversible consumption of quinone (that is, the destruction of the "enzyme"). Accordingly, the proper choice between schemes I and II is fundamentally important.

The reaction of the direct reduction of quinone under scheme I is thermodynamically possible for the iodide ion:

$$2 \overset{\text{O}}{\underset{\text{O}}{\bigcirc}} + 2I^- \;\cdots\; \underset{\text{OH} \cdots \text{O}}{\overset{\text{OH} \cdots \text{O}}{\bigcirc}} \; \overset{\text{O}}{\underset{\text{O}}{\bigcirc}} + I_2$$
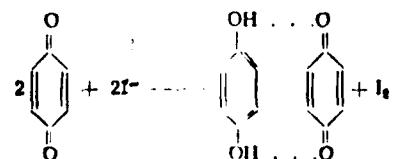
and can be carried out in practice (7). For the bromide and chloride ions the reaction is thermodynamically unprofitable and hence these ions do not reduce quinones. For the hydroxyl ion this reaction is still more unprofitable than for the bromide and chloride ions, therefore theoretically it is of low probability.

Nonetheless, the authors (1) succeeded in detecting hydrogen peroxide in the products of the reaction of quinone with hydroxyl ion, which can serve as proof of the reaction following mechanism I.

In this work an effort was also made to detect hydrogen peroxide in this reaction. Four color qualitative reactions for H_2O_2 were performed: with $KMnO_4$, $K_3[Fe(CN)_6]$, H_2TiCl_6, and with o-tolidine. It was found that the ferricyanide method used in the study (1) is not specific and is not suitable for determination of hydrogen peroxide in this reaction, since hydroquinone present in the reaction mixture yields with this reagent the same color change as does H_2O_2.

It should be noted that detection of hydrogen peroxide by a color reaction in an intensely colored medium and in the present of strong oxidizing agents (quinones) and reducing agents (hydroquinone) is not

possible; therefore, prior to its determination it must be separated from
the reactior. mixture. This was done by distilling it from a neutral or
weakly acidic solution at low temperature. Detection of hydrogen peroxide
was made in a special device where all operations (mixing of solutions of
quinone and alkali, acidifying of the medium, and distillation of the re-
action mixture) can be done in vacuum. Control experiments showed that
in distillation (at the temperature of 0° C) in addition to vapors of the
solvent a certain amount of hydroquinone passed into the liquid nitrogen-
cooled receiver. Therefore, even in distilling the reaction mixture, to
detect the proposed hydrogen peroxide it is necessary to use a reagent
that yields coloration with hydroquinone. The reaction with titanohyd-
rogen chloride acid proved to be the most specific.

Experiments were performed with aqueous and alcoholic solutions
of benzoquinone; the reaction mixture was acidified with acetic or sul-
furic acids. After multiply repeated experiments under varied experi-
mental conditions no hydrogen peroxide was detected in the receiver in
any instance.

In addition, control experiments showed that the method used af-
fords determination of H_2O_2 at a concentration one-hundredth the level
that would be anticipated from equation (I). In these experiments with
H_2O_2 all the operations were executed that were carried out with the re-
action mixture.

Independently of the above described experiments, we have shown
experimentally that hydrogen peroxide cannot coexist with semiquinone.
Various amounts of H_2O_2 were added to a mixture of equimolar amounts of
quinone and alkali and the decrease in semiquinone concentration was
determined by electron paramagnetic resonance (Figures 1 and 2).

From Figures 1 and 2, in which the results of experiments with
methylnaphthoquinone are shown, it can be seen that two equivalents of
H_2O_2 lead to the rapid destruction of 90% of the semiquinone. The ob-
served effect cannot be the result of the displacement of equilibrium
in the reaction

$$2 \; \text{[O=C6H4=O]} + 2OH^- \rightleftarrows 2 \; \text{[O-C6H4-O}^-\text{]} + H_2O_2, \qquad \text{III}$$
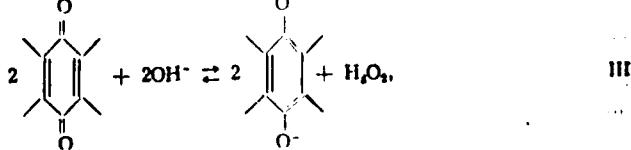
since on the supposition of this equilibrium the semiquinone concentra-
tion as a function of excess H_2O_2 must be governed by a wholly different
law (Figure 2, curve 2) than has been observed in experimentation (Figure
2, curve 1).
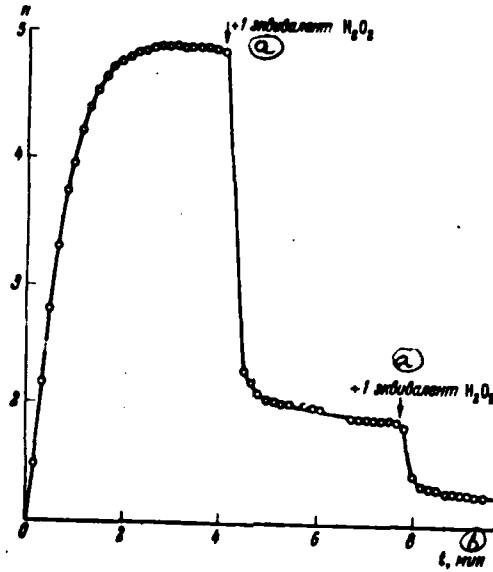
Figure 1. Kinetic curve of the action of H_2O_2 on semiquinone obtained from one equivalent of methyl-naphthoquinone.
Ordinate axis -- concentration of free radicals;
(n) = arbitrary units.
LEGEND: a) + 1 equivalent H_2O_2; b) minutes.

The action of hydrogen peroxide on semiquinone leeds evidently to its oxidation to quinone, which under reaction conditions undergoes rapid irreversible transformations (8) (cf scheme II). In the case of durosemiquinone in weakly alkaline solutions oxidation can be established at the stage of stable duroquinone; when sodium metal is added to the reaction mixture the corresponding semiquinone is obtained once more. These results show that H_2O_2 in the reaction of quinones with alkali would never be detected even in the case if the reaction followed scheme I, since hydrogen peroxide reacts rapidly both with the original quinone (8) as well as with the semiquinone.

Comparing schemes I and II, we can see that under scheme II tetrasubstituted quinones cannot react with hydroxyl ion with the formation of semiquinone, while under scheme I all quinones exhibiting sufficiently high redox potential are capable of this reaction. Thus, comparing the reactivity of quinones that have even one ring proton and tetrasubstituted quinones, we can make an unambiguous choice between mechanisms I and II.

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Study of the reaction of the hydroxyl ion with ten different
quinones that have from one to three ring protons showed that the form-
ation of semiquinones in alcoholic alkali as a rule occurs almost in-
stantaneously; in an aqueous medium in many cases the reaction rate
is reduced, which can in part be related to the low solubility of qui-
nones in water. 2-Methylnaphthoquinone and 2-n-methoxyphenylnaphtho-
quinone react most slowly; the maximum yield of semiquinone in alcoholic
alkali in these cases is attained in one to two minutes.

Figure 2. Action of H_2O_2 on semiquinone
obtained from one equivalent of methyl-
naphthoquinone.
1 -- curve for experiment; 2 -- function
computed on assumption of displacement
of equilibrium III; 3 -- function com-
puted according to scheme II. Ordinate
axis -- quantity of free radicals as %
of original amount.
LEGEND: a) equivalents of H_2O_2.
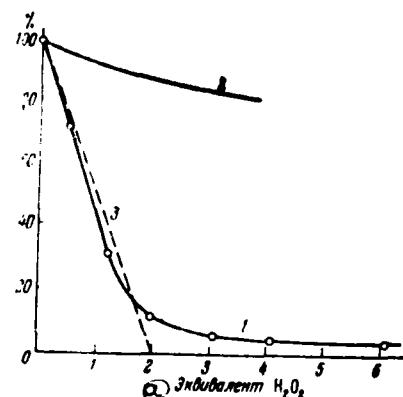
        Tetrasubstituted quinones, in particular, tetrachloro- and tetra-
fluoroquinone, do not form the corresponding semiquinone with alkali in
aqueous solution. in spite of the fact that according to scheme I tetra-
chloro- and especially tetrafluoroquinone under these conditions must
react most energetically with the OH⁻ ion.

        It is important to note that the signal of the corresponding
semiquinones in this case arises immediately after the addition to the
reaction mixture of organic compounds (alcohol, dioxane, and acetone).
Duroquinone in the presence of a large excess of KOH behaves in the same
way. Thus, formation of semiquinones from the indicated tetrasubstituted
quinones occurring in water-alcohol and water-dioxane solutions occurs as
a result of their reduction by organic compounds, which has nothing in
common with the process in question.

        Vicasol and anthraquinone upon standing for 30 minutes in water-
alcohol solutions in the presence of one and a half equivalents of al-
kali also do not form semiquinones. The electron paramagnetic reso-
nance signal of semiquinones from vicasol is formed slowly only in al-
coholic and water-alcoholic solutions containing a large excess of alkali.

        These results are a convincing argument in favor of the nucleo-
philic substitution mechanism according to scheme II.

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Reactions of quinones occurring under scheme II have been well studied (9, 10). When various nucleophilic agents (RSH, CN⁻, R₂NH, etc.) act on quinones, the corresponding mercapto-, cyano-, and aminoquinones are isolated. Under the above-stated scheme, upon the reaction of quinones with the hydroxyl ion, formation of oxyquinones would be expected; the literature contains only indirect data indicating their presence in the reaction mixture (11).

Silica gel chromatography was used by the authors to observe directly formation of 2-oxynaphthoquinone upon the reaction of naphthoquinone with alkali. The reaction was conducted in a sealed vial in the total absence of oxygen, in a water-dioxane solution (1:3). The concentration of reagents is 10^{-3} M. Ten minutes after the alkali has been added, the reaction is inhibited by acidifying with sulfuric acid. Then in vacuum at low temperature and without access to oxygen the solvent is distilled off; the precipitate is dissolved in benzene and subjected to chromatography on silica gel.

A counter-current synthesis of this compound using the well-known method (12) was conducted for identification of 2-oxynaphthoquinone in the reaction mixture. Both compounds obtained have the same Rf value upon chromatography on silica gel-coated plates, and also in ultraviolet and infrared spectra; the latter have characteristic absorption bands of the aromatic oxy-group in the region of 3180 cm^{-1} and of two nonequivalent carbonyl groups of the quinone in the region of 1647 cm^{-1} and 1684 cm^{-1}.

Under scheme II, we would anticipate that in solutions of various alcohols upon the action of the corresponding alcoholates on quinones alcoxy-derivatives will be obtained instead of oxyquinone. Actually, after a sixfold excess of alcoholate is poured into the benzoquinone solution a n-benzosemiquinone signal arises immediately; in 5-10 minutes it wholly disappears and the electron paramagnetic resonance spectrum of the corresponding dialcoxysemiquinone appears:
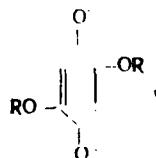
where R = CH_3, C_2H_5, and C_3H_7.

The dynamics of the process affords acceptance of the assumption that the occurrence of these compounds is due to the reduction of the corresponding alcoxyquinones by means of relatively slowly occurring polymerization reactions (of below).

When $R = CH_3$, the spectrum contains seven components with a binomial ratio of component intensities of 1:6.6:15:20:13.7:5.8:1.1 (theoretically 1:6:15:20:15:6:1), corresponding to the reaction of the unpaired electron with six protons of methoxyl groups (reaction with ring protons proves to be many times more limited). When $R = C_2H_5$ and C_3H_7, the spectrum contains five components corresponding to ultra-fine splitting into four alpha-protons; the intensity ratio corresponds to the theoretical 1:4:6:4:1.

In conclusion, it must be emphasized that in alcoholic media quinones evidently can react in several directions; here scheme II describes only one of the ongoing reactions. Conditions can be selected in which the reaction occurs mainly under the indicated scheme. The most important factor in this case evidently is the low concentration of reagents and the properties of the solvent[2].

In experiments with naphthoquinone we have observed, using chromatography, that an increase in the concentration of reagents or the replacement of aqueous dioxane for aquous alcohol leads to formation, in addition to very small quantities of 2-oxynaphthoquinone, of significant amounts of naphthohydroquinone and from two to six other compounds. Most of these are readily soluble in alkali and according to infrared spectral data contain an aromatic oxy-group. Based on the fact that $K_2Cr_2O_7$ under mild conditions does not oxidize these compounds, it can be concluded that we are dealing with derivatives of oxyquinones, but not with hydroquinones, since the latter must easily be modified under the action of an oxidizing agent. It is possible that these compounds are formed as a result of processes of di- and polymerization of quinones, which were studied by Erdtman (13) and one of the authors of this present work (14).

It remains unclear whether or not formation of polymers is only a secondary process or a process proceeding in parallel with oxyquinone formation. In the latter case, some of the quinone molecule is reduced not through the reaction with the oxyhydroquinone ion, but through polymerization processes (15). It can be shown that in any case upon the reaction of equivalent amounts of alkali and quinone, the semiquinone yield must not exceed the limits of 50-85%.

Actually, as has already been reported in a study by one of the authors (15), the experimentally found value of the yield in the case of 0.005 M of reagent solvents is 67 ± 6%.

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[2] The carbonate ion also acts strongly on the direction of reactions of quinones in an alkaline medium. In the presence of this compound oxynaphthoquinone is not formed; the electron paramagnetic resonance spectrum of naphthosemiquinone is not recorded in this case, instead, a narrow singlet signal is recorded.

Conclusions

1. Confirmation has been found that quinones react with the hydroxyl ion according to the mechanism of nucleophilic displacement that is usual for this class of compounds.

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